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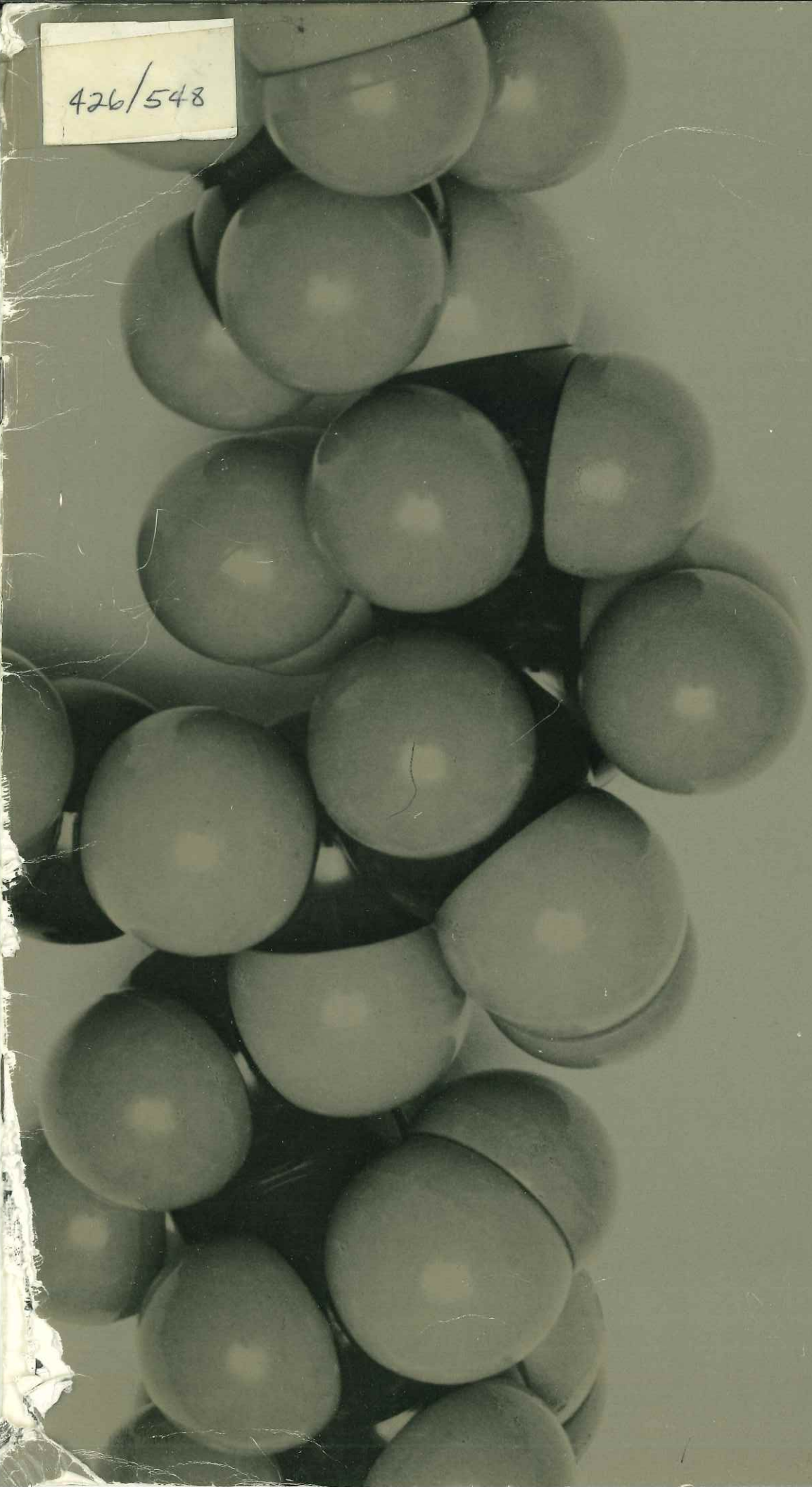


Dynapol

Forging Safer Links in the Food Chain

America's population not only continues to grow, but is becoming more concentrated in urban centers. Providing food in the variety and at the price our people demand is even now taxing agricultural, food processing, and distribution capabilities. Beyond America's food demand lies that of the rest of the world.

Food additives, used to preserve, flavor, and enhance the palatability and nutritional value of foods, are vital to feeding the world's growing population. However, substantial health risks may result from the increasing use of present chemical additives—unacceptable risks that arise because additives are absorbed into the entire human system along with the food.

Just over a year ago, Dynapol was formed to solve this problem through use of a unique technology originated at ALZA Corporation. Our goal is the precise molecular engineering of safe food additives, thereby removing toxicity risk by making food additives nonabsorbable.

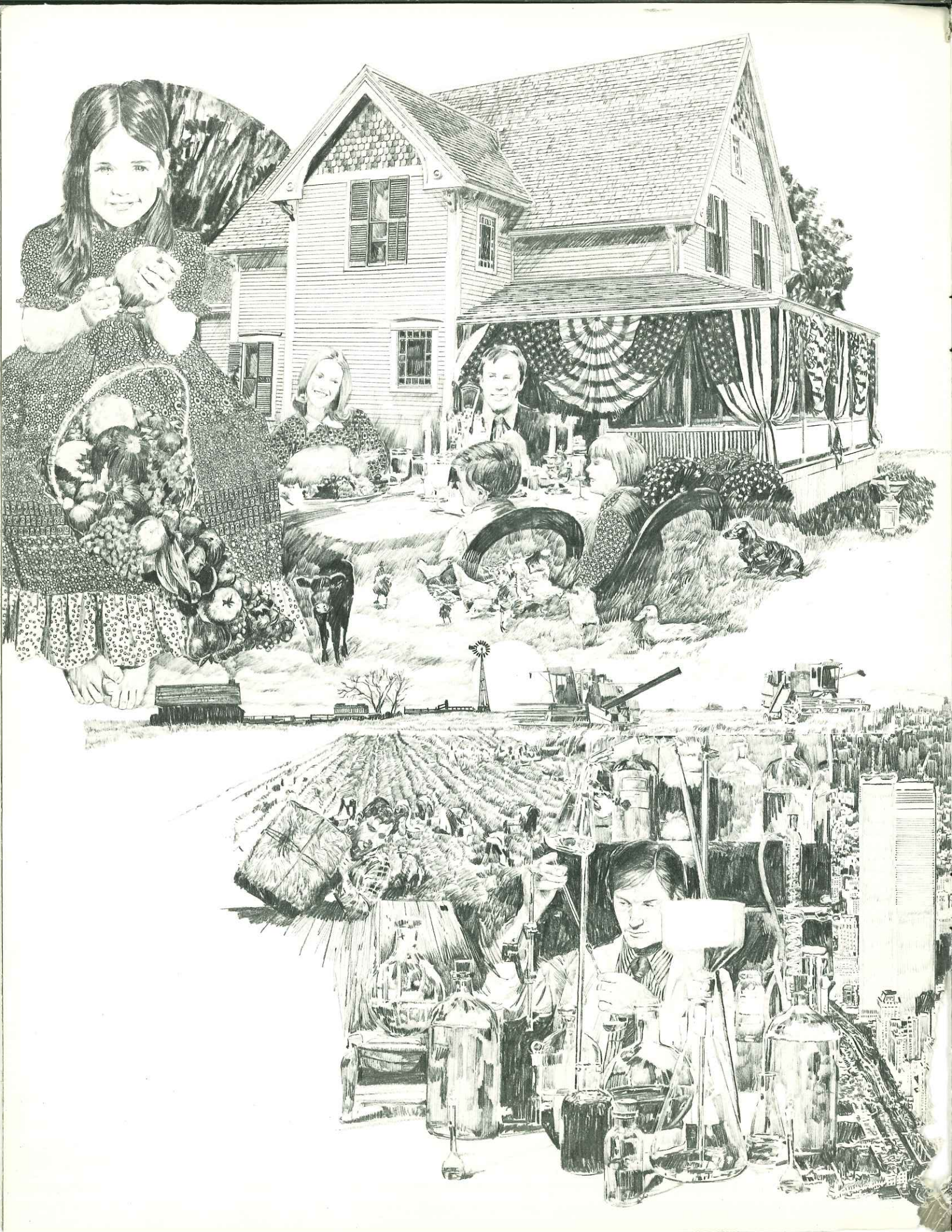
We are well underway towards attaining this goal. In the past year, we have assembled the core financial and physical resources and the scientific, technical and management teams necessary for this, our product development stage. And our research has made rapid progress toward the development of safe food colorings, antioxidants and sweeteners.

In this booklet we will acquaint you with the problems of food additives, how we intend to solve them, and the business potential of our efforts.

DR. ALEJANDRO ZAFFARONI
Chairman of the Board

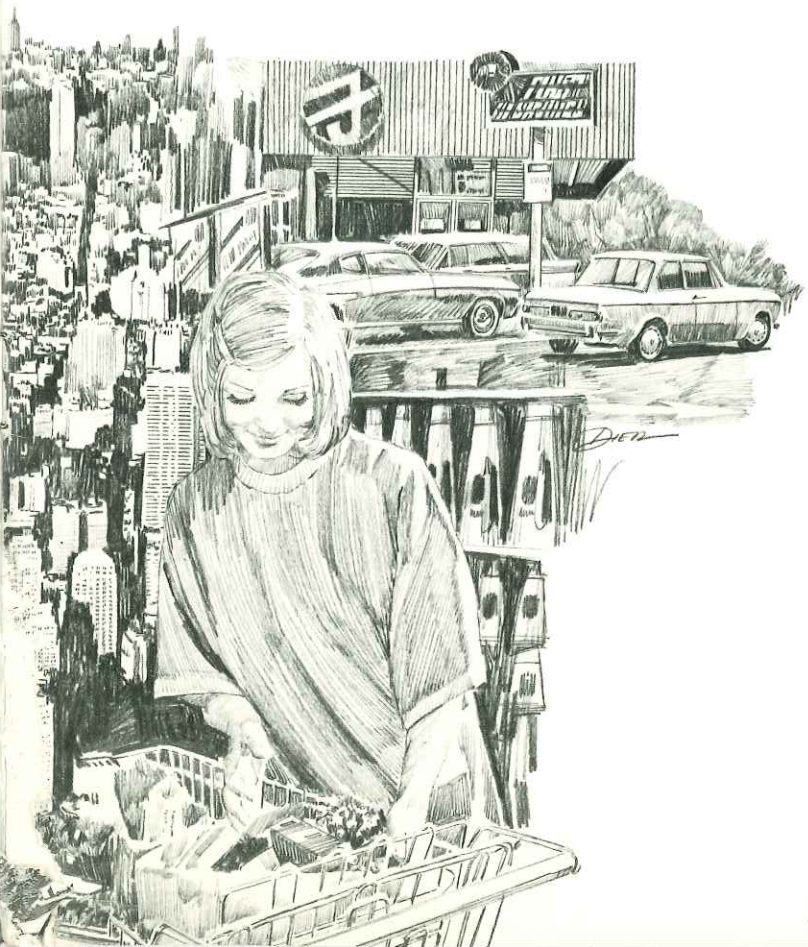
STEVEN GOLDBY
President

August 31, 1973



There's more than food to food today . . .

A century ago, while America was yet a rural society, the country store stocked fewer than a hundred food items, mostly dried staples, along with fresh fruits, vegetables and meats produced by local farmers. What the rural family didn't raise itself was bought at the general store as it was needed, then was prepared and eaten before it could spoil.



Who needs to be told that times—and food—have changed? But let's be realistic in our nostalgia for those simpler days. While we might like to reminisce about sweet fresh peas from the backyard garden, let's not forget how much of the year they were out of season. While we can daydream about thick cream and cool buttermilk from the family cow, let's not forget milking before the winter dawn, cranking the separator and tending the livestock. That crusty bread, warm from the woodstove oven, bore the cost of gathering and splitting the wood, and a day's labor in the hot kitchen. The joys of life at the turn of the century are worth recalling. But we should not ignore the dawn-to-dark toil that was required simply to shelter, clothe and feed the family.

By 1940, the average grocery store stocked well over a thousand items and homegrown foods were beginning to take a back shelf to processed ones. The supermarket became a way of life by 1950, and today, the aisles of the market are overflowing with thousands, often tens of thousands, of items.

Americans have come to expect economy, high quality and ease of purchase, as well as convenient nutrition. Our population has grown rapidly, straining our agricultural, processing, and distribution resources.

Nostalgia must give way to reality. *We cannot feed 210 million Americans concentrated in the cities by producing and marketing foods in the old way.*

Additives are here to stay

To meet this country's nutritional needs at a time of rapid population growth and urban concentration, and to satisfy consumer demands, food processors have had to rely on chemical additives at an increasing rate and of an increasing variety. At present, an estimated 2,500 food additives are in use, accounting for half a billion dollars in annual sales in the U.S. alone.

Properly used, additives have contributed significantly to the processors' ability to get healthful, tasty, satisfying foods to the family of the seventies. In bread, emulsifiers

retard staling and preservatives prevent mold. Antioxidants prevent peanut butter, shortening, and margarine from turning rancid. Vegetable gum stabilizers keep ice cream from melting too fast, in addition to maintaining its texture. Salt would cake up if it were not for a silicate additive. Additives have allowed the development of such convenience foods as flavored cake mixes, powdered juice bases, frozen dinners, dehydrated potatoes, dry cereals, non-dairy creamers, diet soft drinks and foods, and pancake mix.

While additives have become important to the processing of foods in America, they are vital to ending the food supply crisis in developing nations of the world. To feed these growing, sometimes starving, populations, food producers have had to turn to other than traditional foods. These include newly developed sources of nutrition, such as fish meal and proteins prepared by fermentation processes. Such foods are highly nutritious and, as the world population continues to grow, they will have to be utilized more. But to make them palatable and acceptable to people who have strong cultural biases to particular kinds of foods, additives are essential—to flavor, to texture, to color, to preserve.

Additives can be toxic

Unfortunately, with convenience, longer shelf life and taste appeal, comes the risk of toxicity, brought about by life-long exposure to food additives. Only recently have major efforts been directed to determining what health problems may be caused by the five pounds of additives a year that the average American now ingests. Some food additives have shown significant toxic potential and, as a result, have been eliminated from our food supply. The government-approved "generally recognized as safe" (GRAS) list of food additives is under scientific scrutiny. All of these substances now are being reviewed by the U.S. Food and Drug Administration to determine if they are safe.

We can be certain that there is more than nutrition to food today. There is a risk of long-term toxicity caused by repeated exposure to high levels of some additives.

This danger has not entered our food chain overnight. Some risk was always there. Preservatives of one kind or another have been used in foods since far back in the reaches of human history. Brine and smoke, seaweed and starch thickeners, herbs and spice flavorings, plant extract colorings, and flavor enhancers made from fish, all have been used for ages. These may be innocuous, but few have been thoroughly studied. Sassafras, a spice once used to flavor root beer, was found to contain a toxic chemical, safrole, and was banned in 1960 when it was demonstrated to cause cancer of the liver; in 1967, oil of calamus, a natural flavoring, was found to cause tumors in test animals.

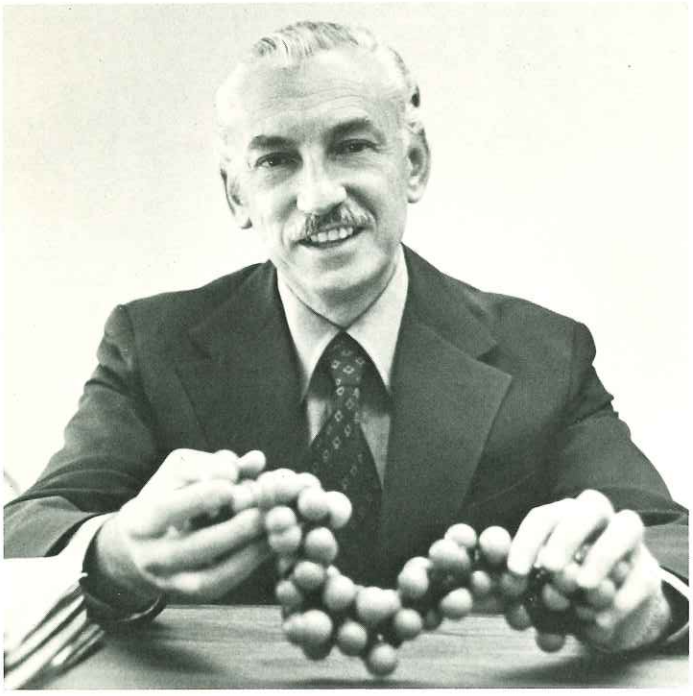
Today, the risk has multiplied. Since our ability to measure the biological impact of additives has improved, we now can be more sensitive to the potential hazards of the increased use of these chemicals. Growing concern by scientific groups and government agencies demonstrates the pressing need for innovators to come to the assistance of the consumer through the food processor by developing better, safer additives. *For food additives are not just food additives—they are human additives.*

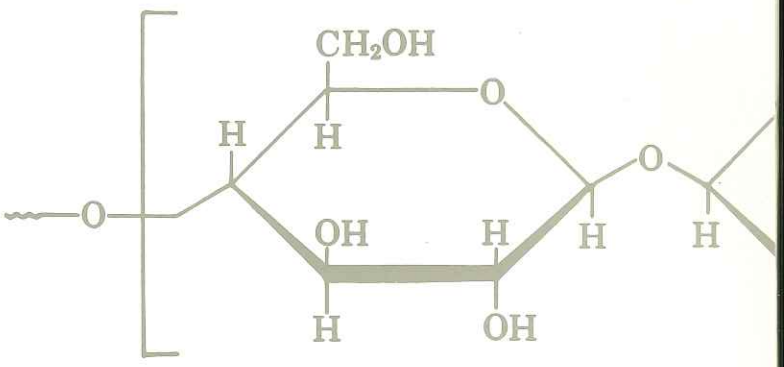
A biological, not a chemical, viewpoint is vital

Now that the consequences of the addition of potentially harmful chemicals to our food are becoming known, the list of permissible additives is being reduced. Solving the problem of feeding an expanding population has increased the problem of maintaining its health in the face of the solution. Yet solving the problem of health hazards by removing food additives from use will present again the problem of providing the required amounts of food with the characteristics we want.

That is where Dynapol comes in—changing for the better this benefit to risk ratio of additives. Dynapol technology is aimed at creating a solution to both problems, at satisfying the wants and needs of both the food processor and the consumer.

Dynapol's First Goal— Eliminate the toxicity of food additives while retaining the benefits





Interview with
ALEJANDRO ZAFFARONI, PH.D.
Chairman of the Board, Dynapol

"Most additives are put into processed foods to do their job before we eat the food—to aid in manufacture, to preserve, to stabilize, to color. Others are there merely to make contact with the taste buds. There is no need for additives to act inside the body beyond that of being detected by the receptor cells of the tongue, in the case of flavorings, sweeteners or thickening agents.

"When toxic effects are caused by additives, they occur in internal organs—principally the liver, the kidneys, and the bladder. They have not been reported to occur in the gastrointestinal (GI) tract—that transportation pipe through the body—because the GI tract is lined with a one-cell-thick envelope, the mucosal layer, that is replaced every few days. Continuous replacement of the lining is a natural mechanism of renewal and defense.

"The problem with additives is that they are absorbed through this lining. When additive molecules enter the systemic circulation, they are distributed to the internal organs where they can cause harm. These additives are made up of small molecules, small enough to filter through the wall of the GI tract in the same manner as the nutrients from food. The process of digestion is, in fact, that of breaking down the molecules of our food into small molecules so they can enter the systemic circulation.

"However, substances we consume that are made up of large molecules that cannot be broken down into small ones are tagged as 'disposable' and pass down the tract and are excreted. Cellulose is an example of this."

How does this relate to Dynapol's objective of engineering safe food additives?

"Dynapol's first goal is to eliminate the toxicity of food additives while retaining their benefits. What we are seeking to do is to prevent the additive molecules from being absorbed into the body through the GI tract. In this manner, the additives will perform their function in the food and nothing more.

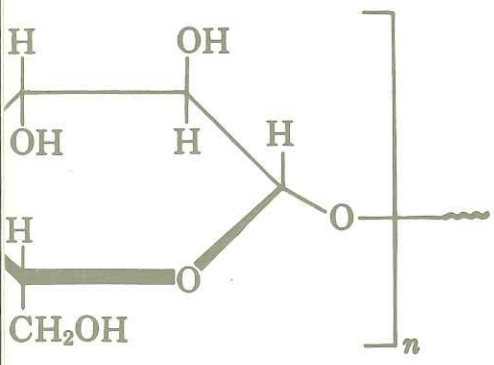
"Our approach to developing safe food additives is to 'leash' the small additive molecules to much larger polymer molecules that won't be able to pass through the gastrointestinal lining."

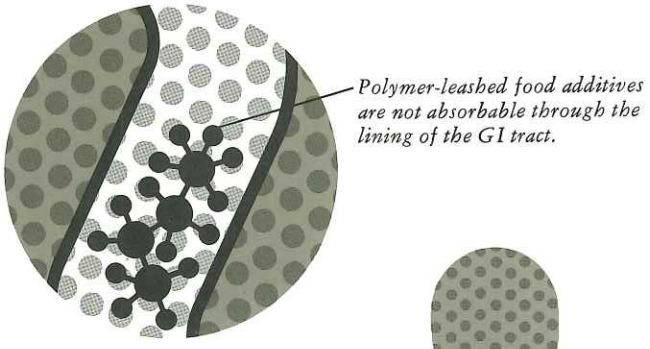
And this leashing of additives to polymer molecules will not affect their action in the food?

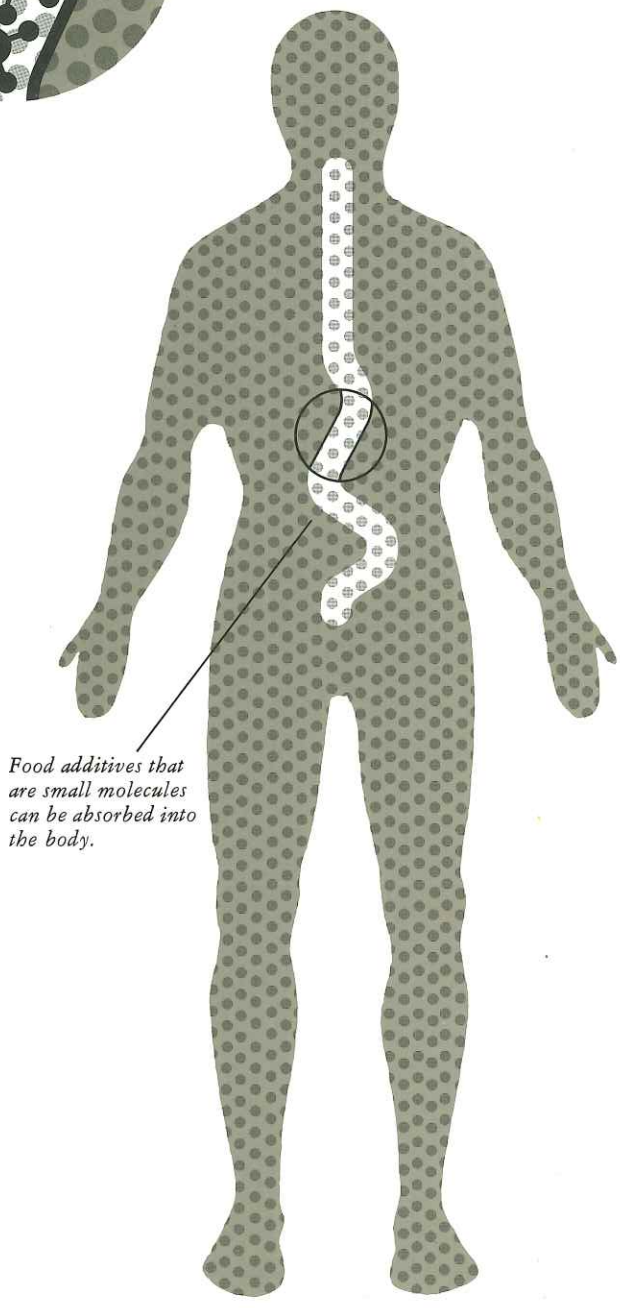
"They will be every bit as able to do their work in the food, but when the food is ingested, the additives will not be absorbed into the body. They will be restricted to going only where their polymer controller goes, down the tunnel of the GI tract to be excreted intact. Along the way, the leash between the additive molecule and the polymer molecule will not be affected by the biological environment."

Let's take flavoring agents. Don't flavors have to be in a small molecule form because the taste perceptor is inside the cell and the molecules have to pass through the cell wall to produce the taste sensation?

"I do not agree with the commonly-held view that the taste receptor is inside the cell. Some recent findings in molecular pharmacology by Dr. Pedro Cuatrecasas, one of our consultants, show that hormones are active and find their receptors on the outside of the cell membrane. Dr. Cuatrecasas did this work by binding the hormone insulin to a polymer. He found he could still get the same effect that one expects from free insulin.







This work has now been confirmed in other laboratories using other hormones such as ACTH and Bovine Growth Hormone.

"We believe that Dr. Cuatrecasas' findings also apply to flavors and explain the very rapid dynamics of flavor perception. If flavor was an inside-the-cell reaction, we would not perceive it so quickly. Prove it: sip a little sugar water; then some plain water; then the sugar solution again, very rapidly. If the sugar molecules had to get through the cell wall to be perceived, you wouldn't be able to detect the change from sweetness to lack of sweetness so immediately.

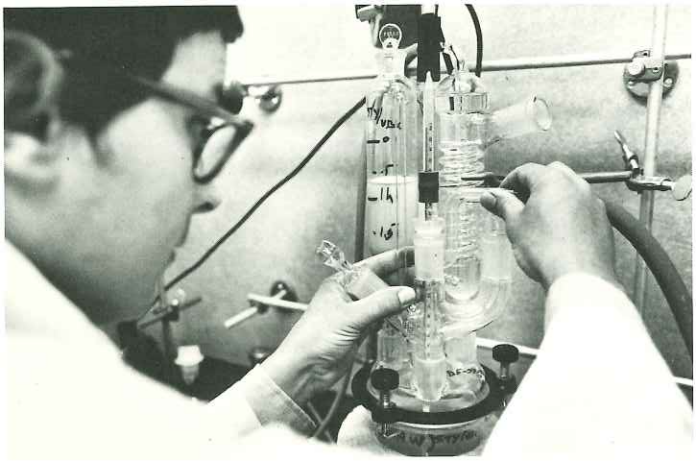
"Because we believe that all flavor and odor perception operates this way, we launched a Dynapol program in this area. A short time later, other investigators reported on a natural polymer that was found to give an intensely sweet sensation. This substance—Monellin—is not a sugar but a proteinaceous polymer, derived from an African berry. Its action on the sweet taste receptor can be likened to the action of the protein hormones on the cell membrane receptor, already discussed. Discovery of Monellin lends support to our concept of flavor perception. This is very important to the application of our molecular leashing concept to flavorings and sweeteners. While the leash will bind the active molecule to the polymer controller, if properly designed, it should still allow it to produce a taste sensation, a result previously not considered possible."

What about the companies making food additives now; haven't any of them taken this kind of approach to the toxicity problem?

"Historically, they have been organized to search out chemicals that might be useful to a particular product and examine them for their existing properties and their relative safety. There has been much modification of existing chemicals and accidental findings, but little preplanning of safe molecular structures.

"Cyclamates and saccharin, for example, did not result from a search for non-nutritive sweeteners. They were found quite by accident during research in other fields. Many of the food additives that are produced by pharmaceutical companies today were by-products of drug research; others have come from chemical firms with positions in agricultural chemicals and additives for industrial products. In contrast to these companies, Dynapol was formed with the goal of applying new technology and scientific advances to the engineering of safe food additives."

Preparation of polymeric food additives



But isn't safety largely a matter of testing and selection of additive chemicals?

"Testing for safety is not a simple matter. There are chemicals that, upon a single administration, will produce a cancer in all of the animals tested. But with some materials, this cancer may not appear until long after ingestion of the single dose. For a time, nothing seems to happen; in the case of the rat, such a tumor may appear six months . . . a year . . . a year and a half later. This corresponds to a longer lag time in man.

"In view of this, it is essential that all food additives be adequately tested for their long-term safety. We believe, however, that it will be surer and safer in the long run to engineer safety into food additives right from the start, with Dynapol's concept of polymer leashing of additives. By rendering food additives nonabsorbable, safety testing will be more accurate and the results more predictable.

"Our approach is not simply one of molecular engineering, but is primarily biological. The advances in food processing techniques may have outstripped our natural biological safeguards. I believe in science's ability to restore the balance by coming to the defense of the biological processes on which the preservation and continuation of health depend. Dynapol's efforts will be based on an understanding of the physiology of the human body and careful attention to the significance and complexity of life processes. There is a problem with current food additives, a biological problem, and we intend to solve it."

Antioxidants

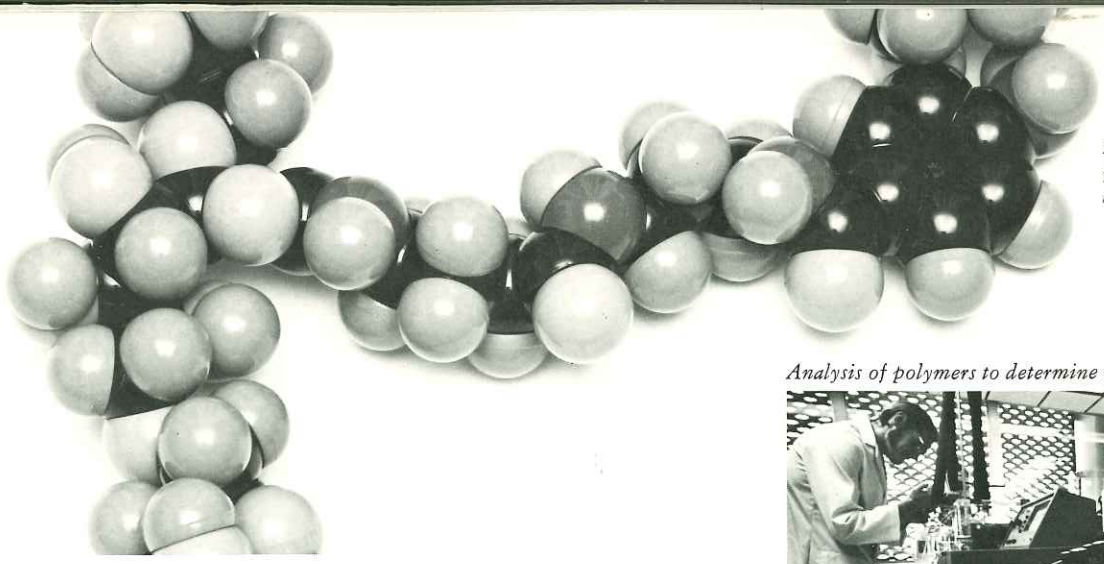
There are probably no food additives used as ubiquitously as the antioxidants. Oils and fats have natural antioxidants in them, but these are destroyed in processing and must be replaced for the food to retain its freshness. Without antioxidants, shortening becomes rancid, citrus oils taste bitter, chewing gum becomes brittle, vitamin A loses its potency and even paraffin wax develops an unpleasant odor and flavor.

Butylated hydroxytoluene (BHT) and butylated hydroxyanisole (BHA) are commonly used antioxidants. They are added to bacon, cream, shortening, processed meats and fish, baked goods, margarine, salad oils and dressings, nuts, raisins, milk, whipped toppings, imitation fruit drinks, breakfast cereals, spices, pet foods, beverages, chewing gum, cosmetics, drugs and many other items. They are also used in food-packaging materials for cottage cheese, ice cream, potato chips, cereals, cookies, bread, butter and cheeses—even in household wax paper.

BHA and BHT remain on the FDA-approved "generally recognized as safe" list. They are important additives for the preservation of food and its fresh flavor. They also protect some of the natural vitamins in food. However, the toxicity risk they bear in their present form may be too high, compounded by the cumulative amounts one is exposed to by ingestion over a lifetime.

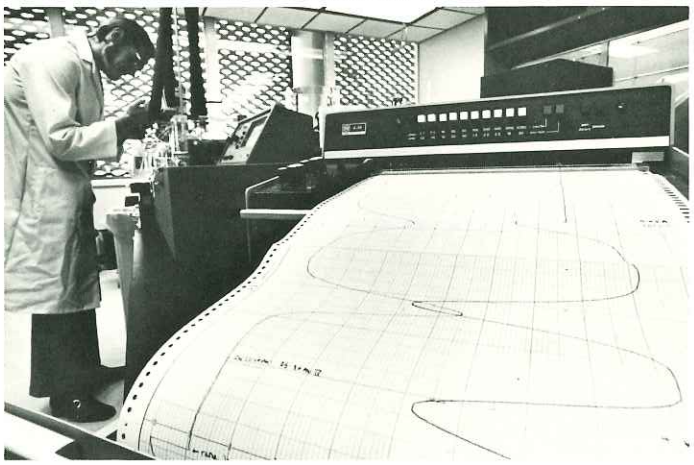
Food colorings

Coloring makes foods more acceptable to the consumer. In many cases, coloring is used to restore the natural color lost in cooking or canning or through enzymatic action when fruit is peeled. The very real contribution to palatability brought about psychologically through the use of coloring can perhaps best be illustrated by the history of margarine in the United States. Uncolored at first, margarine was equated with lard; it was only after introduction of the familiar yellow coloring that margarine began to displace butter in the diets of many consumers.



Molecular model of polymer-leashed food additives.

Analysis of polymers to determine molecular weight



Food dyes, unfortunately, are not all innocuous. Since 1960, almost a dozen previously acceptable dyes have been withdrawn from use in food. At present, there are only eleven synthetic dyes that can be used for food coloring. Because of toxicity, three of these are only permitted to be used in one type of food each.

Violet 1, the dye used by the government to stamp meat, was withdrawn in April of this year. Japanese studies showed it to be carcinogenic in animals. Now it seems that at least one more of the remaining dyes may be toxic. Red 2, the most widely used food coloring, has caused toxic effects in animal tests. The FDA is currently evaluating proposals to restrict its use to certain non-beverage foods or to ban it entirely.

As the list of permissible dyes is shortened, the food processor eagerly awaits a new spectrum of safe food colorings. These colorings must be provided for the present variety of processed foods to remain available.

Non-nutritive sweeteners

The ability to perceive sweetness served a useful purpose in man's early relationship with nature, attracting him to fruits and berries that were rich in vitamins and minerals. But man quickly came to want more sweetness than he needed, and more convenient sources than berries. Satisfaction of this craving for sweetness may present health problems of as yet undetermined magnitude.

Sugar cane, from which we get two-thirds of our sugar, originated in Northeastern India and was carried to Egypt and China fifteen hundred years ago. It is not generally realized that sugar is a relatively new constituent of the human diet, used widely for only 100-150 years. Columbus introduced sugar cane to the West Indies in 1494. By 1880, machinery had been devised to refine sugar with a long shelf life, cheap enough for almost anyone to afford. Our per capita consumption of sugar has increased seven-fold in the past century. Worldwide, U.S. consumption is among the highest. Currently, the average American consumes 100-130 pounds of sugar a year and the trend is still up; we soon may be consuming half a pound of sugar a day, on the average, knowingly or not. Candy can be almost 50% sucrose, but not all sources of sugar are so obvious; sugar also is present in such food products as salad dressings and soups.

Though few consumers make the distinction, sugar and starch as energy sources are two quite different things. In starch, the glucose (a natural sugar) is polymerized into polysaccharides. There is a time process of disengaging glucose from the starch polymers in our diet, so that its absorption into the bloodstream is slow. But cane sugar or sucrose splits into fructose and glucose on digestion. These are tiny molecules that are rapidly absorbed into the bloodstream through the lining of the GI tract.

We used to eat just a few times a day and there was less sugar in our meals then. Today, many snack constantly on sugar-sweetened products. One candy bar is the carbohydrate equivalent of five slices of bread, but its sugar is almost immediately "pulsed" into the system.

This presentation of sugar presents some potential health hazards. If we "pulse" glucose many times a day, as we do with candy, soft drinks, sweetened coffee, or other foods sweetened with sucrose or corn syrup, the body responds by releasing insulin in pulses, too. And insulin can be a toxic substance when it is called for repeatedly in this manner. Insulin has an effect on the fat tissue, triggering the release of fatty acids. There may be a correlation between high sugar intake and the prevalence of atherosclerosis, a precursor to the increasing incidence of heart attacks.

These and other consequences of our high consumption of sugar indicate that there is a need for other, safer sweeteners.

Creation of non-toxic, non-nutritive sweeteners could help us deal with the problem of obesity caused by unneeded and unwanted calories. And it could allow us to diminish the possible disease consequences of the continual pulsing of sugar throughout the day by a population accustomed to a good deal of sweetness in their lives.

Synthetic sweeteners, of course, have been with us for some time. In 1879, saccharin was synthesized. It was intensely sweet—300 times sweeter than sugar—inexpensive and not bulky to handle.

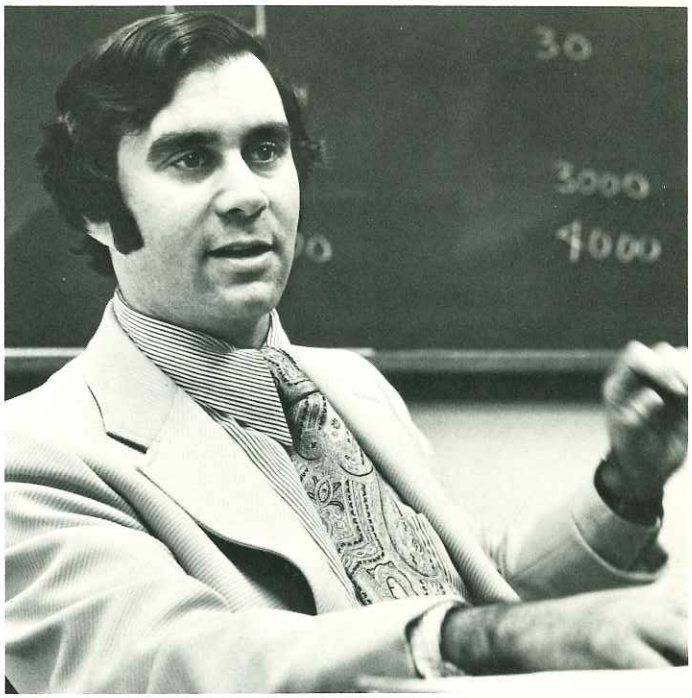
In 1950, cyclamates were found. Thirty times sweeter than sugar, cyclamates did not lose their sweetness in cooking, canning or baking.

By 1969, the annual rate of consumption of cyclamates by the American population had reached more than 13 million pounds. Almost everyone was ingesting some of the chemical in soft drinks, gum, sugar substitutes and processed foods. Sales of diet colas sweetened with cyclamates were estimated to total around $300 million annually at wholesale prices. Concern over the safety of the cyclamates began to grow as early as 1960, and they were generally removed from the U.S. market in 1969 after animal studies showed the growth of bladder tumors.

The removal of cyclamates made saccharin attractive once again to food processors and weight-watchers, even allowing for its bitter aftertaste. But saccharin, too, has been implicated in the genesis of bladder cancer. Last year, the FDA limited the food use of saccharin to soft drinks and other beverages; nevertheless, 3.7 million pounds of saccharin were consumed in the U.S. in 1972. Its future is uncertain pending the outcome of additional testing.

The restriction in use of the cyclamates and saccharin has left a huge, unsatisfied market for sweeteners that will do nothing more than sweeten and that are entirely, assurably safe for consumption.

The Dynapol Promise—Safe Food Additives



Interview with
NED M. WEINSHENKER, PH.D.
Vice President/Research, Dynapol

"Our objective is to develop a systematic approach to the design of better food additives, to find universal means that will assure their safety in the human diet at virtually any level of dietary intake.

"Dr. Zaffaroni conceived the idea of leashing additive molecules to polymer controllers. This would preclude the additive from being absorbed into the system because the polymer would be too large to pass through the gastrointestinal wall. The leash will be designed to bind the additive to the polymer in a way that will assure stability throughout the GI tract."

It would seem that Dynapol is attempting to put food additives onto plastics.

"There is a common misconception in your statement. Many people associate 'polymer' with 'plastic'. But plastics are just one form of polymer. The body itself is made up of all kinds of polymers. Proteins, carbohydrates, DNA, and RNA are polymers. A polymer is merely a natural or synthetic compound with a high molecular weight, made up of many—even millions of—repeated linked units. Proteins are polymers of amino acids hooked together in a long chain. Your skin is a polymer, so is your hair; albumin and antibodies are polymers."

Safe sweeteners

How do you plan to achieve the technical goals stated by Dr. Zaffaroni, in, say, the case of sweeteners?

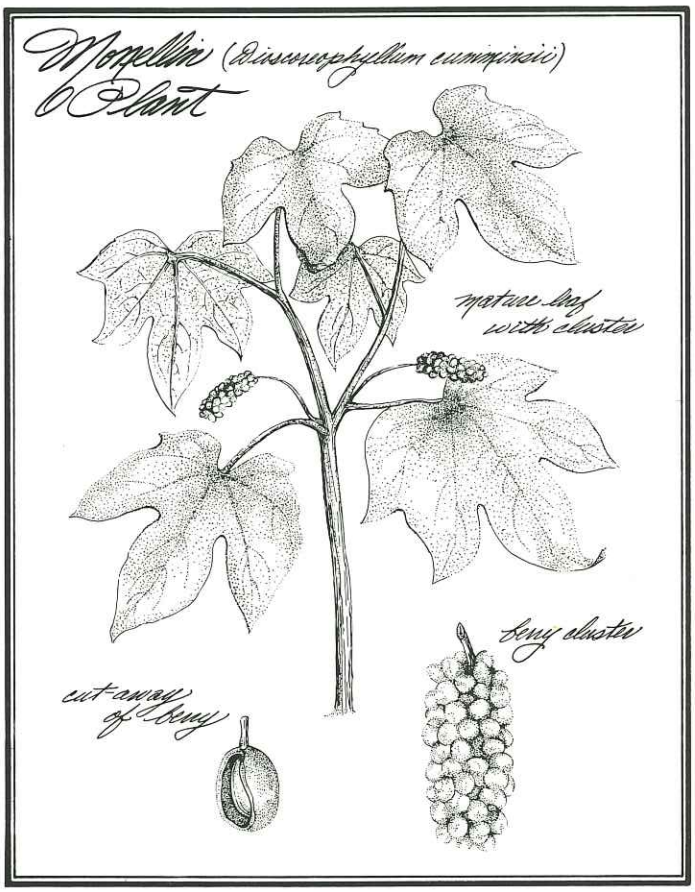
"We have two principal sweetener programs in progress. One has to do with synthetic sweeteners leashed to polymers. Another is concerned with the potential of a rather amazing protein polymer called Monellin, a naturally occurring sweet polymer derived from a berry.

"Let's look at the synthetic sweeteners first. We are attempting to have the sweetener be completely precluded from absorption by the size of its polymer controller. To do this, it is necessary that methods for fractionation of polymeric materials be available, so that low molecular weight species that might be absorbed are excluded. Dynapol has a team of polymer physical chemists who have made progress toward development of this technology."

Can you just take the cyclamates or saccharin as they are and link them to a polymer?

"No, we just can't pick any sweetener off the shelf, make a chemical modification that will allow us to bind it to a polymer, and come up with an acceptable sweetener. It requires much more sophistication and technology than that. All sweetener molecules are extremely sensitive to changes in molecular structure. If one changes just a few atoms or any configuration on the molecule to allow one to attach it to a leash, one generally risks losing its sweet taste. No one has been able to predict consistently the effect of a molecular change in a compound, though we have been able to do this recently in the case of one sweetener group. We now understand enough to realize that the molecule to be leashed doesn't itself have to be sweet; the polymer controller and the characteristics of the leash will have a great deal to do with creating the sweet taste."

Can you discuss further the function of the leash, beyond that of tethering the active molecule to the polymer controller?



"Given a large polymer with the sweetener molecules attached directly onto its surface, the polymer might be so big that it wouldn't be able to approach the cell membrane of a taste cell close enough to allow the sweet molecule to interact with the receptor. Therefore, the leash must be of the proper length to allow contact with the receptor on the outside of the cell membrane. An active molecule too close to the polymeric carrier could not make contact with a recessed receptor cell. But a longer leash should free the active molecule to interact. It's rather like tethering an astronaut to his capsule so he has enough 'play' to explore a nearby object. We're not thinking in terms of feet and inches, of course; we actually tailor the leash atom by atom to the precise length we want."

You mentioned an interest in Monellin. Tell us about it.

"Monellin is a very intriguing substance. It was isolated from a West African wild red berry, *Dioscoreophyllum cumminsii.* It is the first reported protein to be characterized by a sweet taste. As a matter of fact, it is 3,000 times sweeter than sugar and is the sweetest natural substance known. Drs. Cagan and Morris of the Monell Chemical Senses Center at the University of Pennsylvania isolated this soluble, biodegradable protein after four years' work.

"Only small amounts of Monellin were prepared at the Center. However, Dynapol collected larger amounts of the berries during the 1971-72 growing season and is collecting 10,000 pounds this year to prepare large amounts of Monellin for testing in our laboratories and by food processors."

Do you plan to leash Monellin to a polymer in the same way as the synthetic sweeteners?

"We have three programs with Monellin. First, is the evaluation of Monellin itself as a sweetener for foods. Second, is the identification and isolation of the active portion of the molecule. This fragment might then be synthesized and bound to polymeric systems. Third, is the use of Monellin as a model for our synthetic systems."

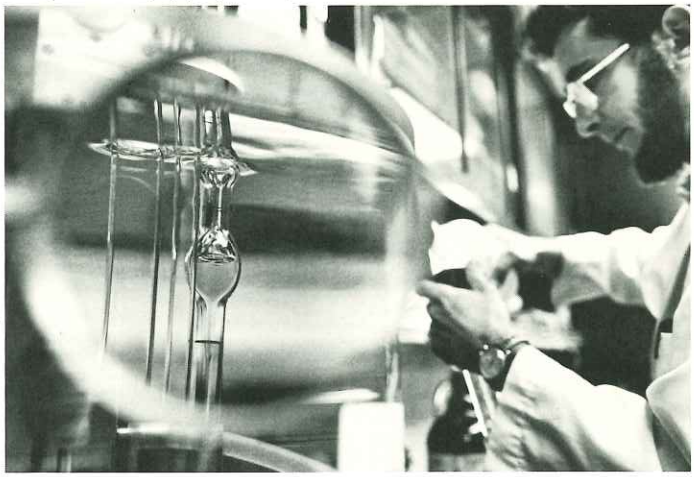
Safe antioxidants

You are also working on antioxidants, Dr. Weinshenker. There seems to be some agitation about the use of BHT and BHA, two of the most common antioxidants . . .

"Critics of BHT and BHA have a right to be concerned. Biochemists in England and the United States have found high levels of BHT in human fatty tissues. We don't know for sure what the effects of this antioxidant level are, but there is evidence that these chemicals in their ordinary form may be harmful.

"On the other hand, processors reason that taking out antioxidants and other additives could raise the price of

Test for viscosity of polymeric food additives



bread by 8-10% and make margarine so unpalatable that it would be unacceptable. With the price of butter what it is today, and the likelihood that a much greater demand could not be met by dairy producers, this could mean a further economic burden on the consumer.

"But Dynapol is working for a third alternative, one that should satisfy both sides of the issue. Data generated at Dynapol and published literature in related fields lead us to believe that attaching antioxidants to nonabsorbable polymer macromolecules will not diminish their effectiveness as preservatives, but will eliminate the toxicity risk. We'll soon know more about this; our first polymeric antioxidants have come out of our laboratories and are now being thoroughly tested. Early test results indicate that two are much more active antioxidants than either BHA or BHT."

Will there be any taste to a polymer-leashed antioxidant?

"BHA and BHT and another commonly used antioxidant, propyl gallate, have poor taste qualities at high concentration. But Dynapol's polymeric antioxidants will be tasteless and odorless."

Isn't there a trend, in breads at least, to have brands with 'No Preservatives Added'?

"Of course, but antioxidants can be put into the packaging rather than into the product. These are called 'indirect' additives. The antioxidant comes off the packaging as a vapor to migrate into the food. Whether or not baked goods contain a direct additive, they often have an antioxidant in their wrappers. Most plastic wraps contain antioxidants, otherwise the wrapping itself wouldn't have a long enough shelf life."

Safe food colorings

You have a program underway in the area of food dyes—how is this coming along?

"Very well. We have made our first oil- and water-soluble polymeric dye compounds. Water-soluble dyes in certain colors are not available for use in food at present. And to date no oil-soluble synthetic dye has been safe enough to be used in foods. It appears to us at Dynapol that our technology can answer the problems of dye toxicity and of lack of oil solubility, and open up the color spectrum for processors."

Will Dynapol's polymer-bound dyes be useful only in foods?

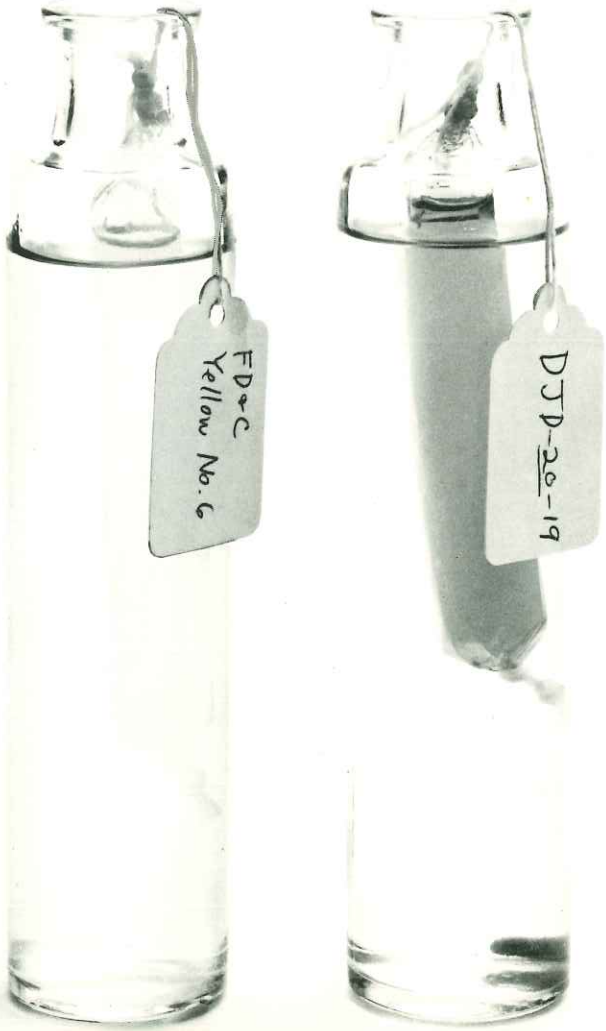
"No, safety of dyes is a concern in more than foods—for example in drugs and cosmetics. Color in lipsticks may be ingested and should be nonabsorbable. Color on the eyelashes and eyelids should not affect the eyes.

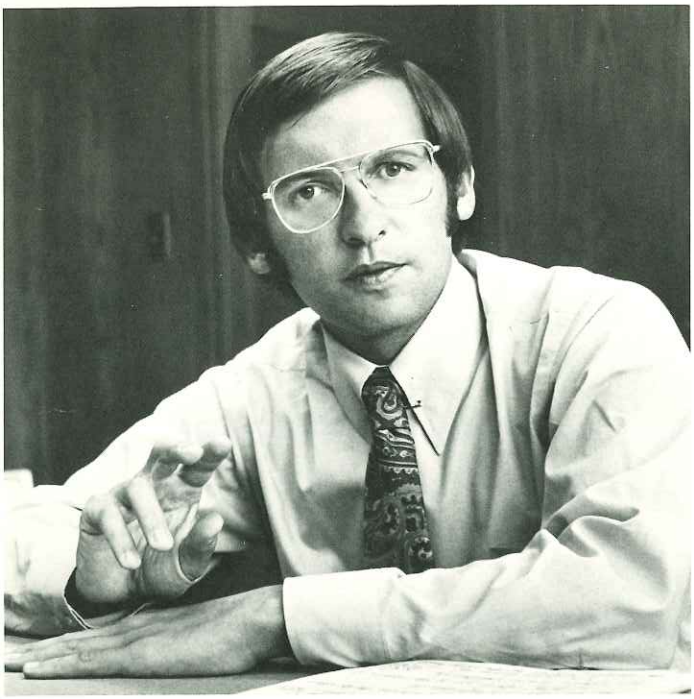
"However, our first interest is in the use of dyes in foodstuffs. Our polymer know-how will be a foundation of common technology and we can expect its application to many products besides foods."

So Dynapol in time may move into other fields besides its involvement with food additives?

"Now we are seeking to engineer safer links in the food chain. But our activities will go well beyond an involvement with food additives. I have mentioned the application of our technology to cosmetics; we can foresee an important role for Dynapol in pharmaceuticals, as well."

Presently used food coloring (on left) passes through the pores of a dialysis bag and into the surrounding solution, while Dynapol's polymeric food coloring (on right) does not.





Interview with
STEVEN GOLDBY
President, Dynapol

"The first stage of Dynapol's development took place at ALZA Corporation. While performing research in other fields, we became aware of the need for improving food additives. When Dr. Zaffaroni conceived of making additives non absorbable by leashing them to larger molecules, we saw a strong business opportunity in developing a line of safe food additives. Basic work was begun in late 1971 and the results of this work were very promising.

"When we studied the alternatives for further developing and commercializing the polymer-leashed active molecule concept, we decided that this could be done best within a separate company. Through this framework, one can aggregate the technical and financial resources needed, without distracting the original company from its primary goals. A new technology or a new application of one already developed can best prosper by giving the people involved the excitement and incentive that a new company environment creates. ALZA itself is an example of this approach.

"So a separate company, Dynapol, was formed in July 1972. It was intended from the outset that Dynapol would be a truly independent entity, with its own goals, programs, management and facilities. A private placement of common stock and warrants funded the new company with $6 million in equity capital. ALZA retained two-thirds ownership."

Could you tell us what has taken place since that time?

"Since then, we have successfully combined a highly qualified and imaginative group of scientists and business managers into a team with capabilities unusual to food additive development. We are bringing a new viewpoint, new disciplines and fresh ideas to bear on an important aspect of the persistent problem of feeding the growing populations of the world. In this short time, a number of promising compounds have been defined and made. Their syntheses are being scaled-up to provide us with larger quantities and initial testing is underway. We are now convinced that the basic concept is workable.

"Dynapol is housed in a modern 30,000 square foot laboratory and office building in the Stanford Industrial Park in Palo Alto, California. This building contains all required laboratory facilities.

"Our next stage of corporate development at Dynapol has already begun. We have broadened Dynapol's management team. With completion of the company's initial phase and to meet the increasing management demands, Dr. Zaffaroni has turned over to me the position of President and Chief Executive Officer. As Chairman, he continues to play a vital role, especially in the scientific area where his ability to conceptualize new ideas gives the company its unique advantage. In July of this year, I resigned my positions as Senior Vice President of ALZA and President of Alza Pharmaceuticals to devote all of my time to Dynapol."

What do you plan for Dynapol to accomplish over the next year or two?

"We are now moving into the product development stage. Dynapol's present programs are directed to specific food additive products with well defined characteristics that will fulfill existing market needs, and market needs that are growing. Antioxidants, sweeteners and dyes are very much in this category and Dynapol's first

objective is to develop and market successfully a line of these safe food additives.

"Dynapol intends to become an important contributor to the food processing chain by providing unique additives that will permit safe processed foods, and protect and enhance desirable food characteristics.

"But we're not just after the replacement of existing additives with safer Dynapol products. There is also a major opportunity for products where there are presently none to fill existing needs. The food coloring area is a good example of this; many colors simply are not available to the processor at the present time.

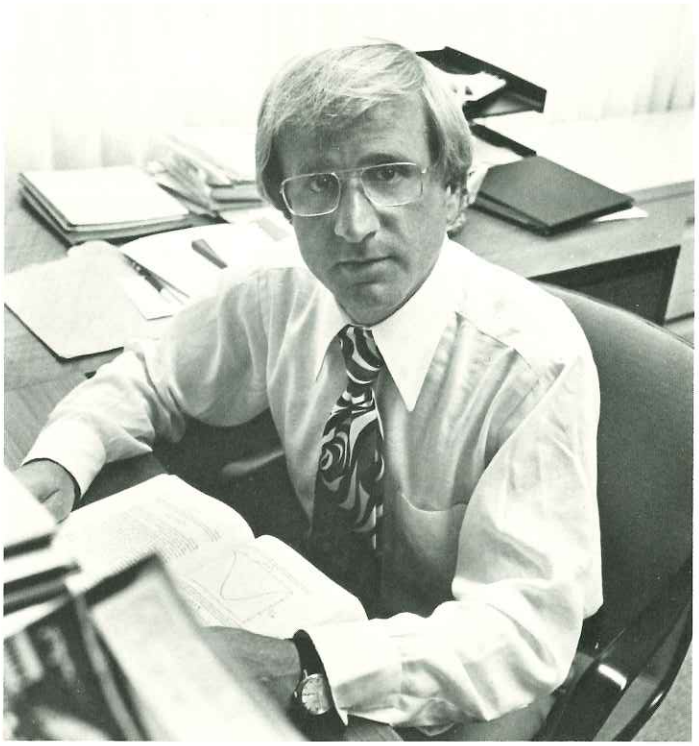
"Of course, a great deal of work remains before Dynapol's technology can be commercialized. Testing has to go forward in several areas. Before our food additives can be marketed, they must be subjected to extensive toxicity testing and be approved by the U.S. Food and Drug Administration. But Dynapol's product development progress confirms our early enthusiasm. We look forward to the future with an expectation of substantial growth and success in the food additive area."

What do you foresee as the long-term applications of Dynapol's technology?

"For food use, Dynapol's technology could lend itself to development of products such as antimicrobial agents to prevent food spoilage . . . flavorings never before possible . . . enhancers that will bring out natural flavors without adding their own . . . even agents that block the sweet receptor, so that the dieter will lose interest in sweets.

"Those are some future possibilities in the food field. But for the longer term, we look at Dynapol this way: our concern is with the 'compartmentalization' of molecules interacting with biological systems. We have now entered the first phase of our endeavors—space control of food additives through the use of polymer controllers. Related approaches will be applied later to other biologically active molecules in areas other than that of the food additives.

Dr. William Leonard, Director of Polymer Sciences



Dynapol scientists are designing means to direct and confine such molecules to act only on the target site where they are needed."

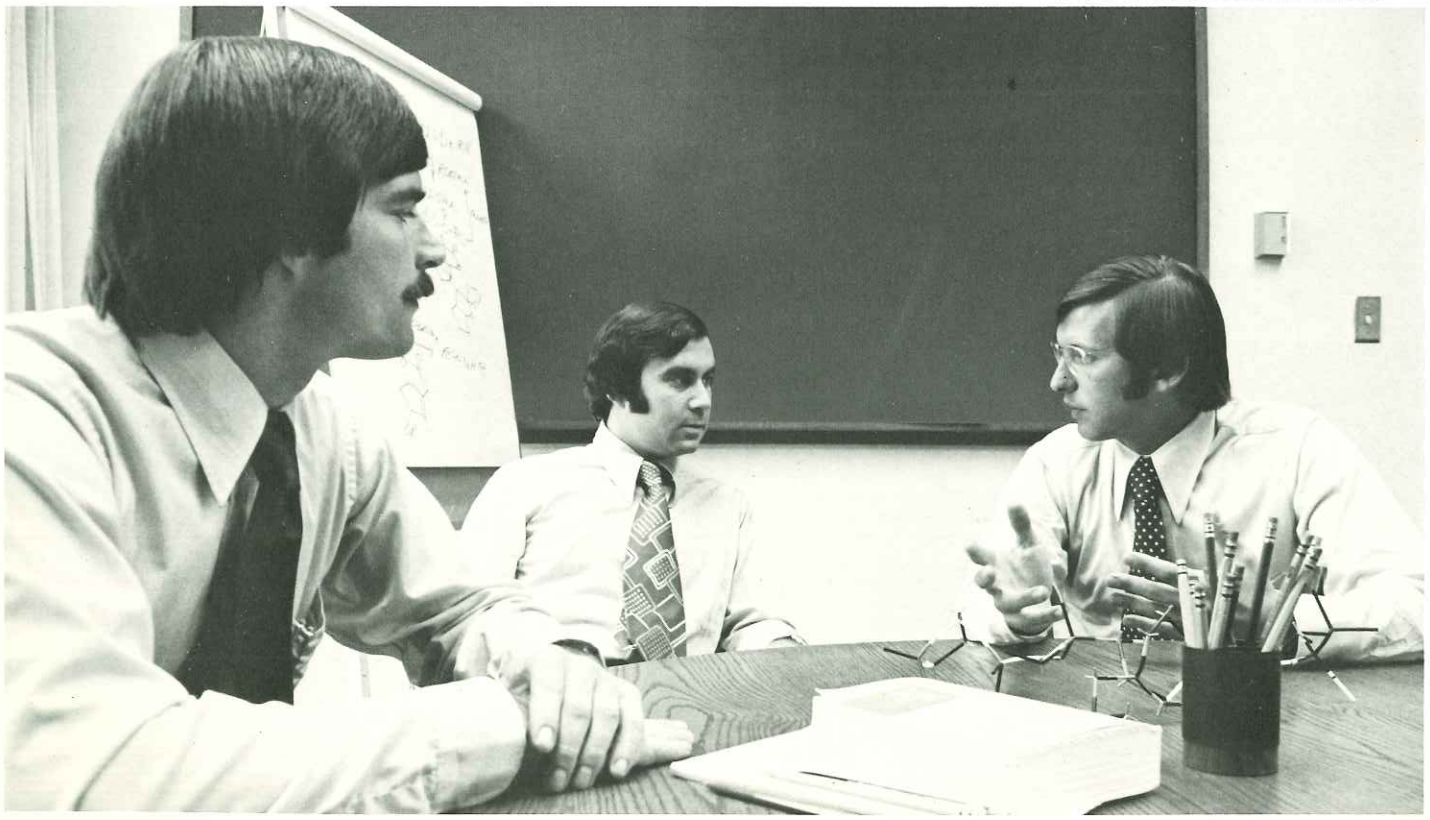
What further can you tell us of Dynapol and its future?

"I would like to give you my personal view of Dynapol, one that makes my own job a uniquely satisfying one to me. Our business was formed with the purpose of solving a specific worldwide social problem—the growing human need for safe food additives. We have made significant progress toward this goal by applying to this problem a new technology.

"It has been satisfying not only to see the technology be embodied in specific product candidates, but also to see clearly the potential for the development of a growing, profitable business. The first phase of our business plan, development of safe food additives, will entail full use of our resources for some years to come. When that phase is completed, we will seek further opportunities through application of our technology to other equally promising fields."

Dr. Guy Crosby (standing), Director of Organic Chemistry

John Poitras (on left)
Vice President—Corporate Development
at planning meeting with
Dr. Weinshenker and Mr. Goldby.



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